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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,968	02/13/2002	Heinrich Wieland	70301/56970	6225

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EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,968	WIELAND ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-52* is/are pending in the application.

4a) Of the above claim(s) *46 and 49-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-45,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6 pages*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 27-52 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 27-40, on February 19, 2004 is acknowledged. The traversal is on the ground(s) that unity of invention exists for the subject matter present in claims 27-40, 41-45 and 47-48 because the inventions of these claims share the technical effect of stabilization, increase and/or decrease of collagen. This argument is found persuasive and claims 41-45 and 47-48 will be rejoined with Group I.

Claims 46 and 49-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on February 19, 2004.

Applicant's election of specie on June 24, 2000 is acknowledged the specie election: (1) 4-hydroxyandrostenedione (aromatase inhibitor, (2) Tamoxifen (anti-estrogen), (3) 4-hydroxyandrostenedione , (4) not identified, and (5) 4-hydroxyandrostenedione (a 5-alpha-reductase inhibitor that inhibits the production dihydroxytestosterone. The election was made without argument or a statement of traversal. Therefore, the election of specie is considered to be without traverse. The election of specie will be applied to the rejoined claims.

Claims 27-45 and 47-48 are presented for examination.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 27-31, 24 and 38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-7 of U.S. Patent No. 6,071,526. Although the conflicting claims are

not identical, they are not patentably distinct from each other because '526 is drawn to a method of treating cellulite comprising applying an aromatase inhibitor, an anti-estrogen or both to skin to improve subcutaneous connective fatty tissue disturbances. This method is a specie of the instant claims which are drawn to a method for the stabilization, the increase or the restoration of collagen in a mammal comprising administering an effective amount of a substance which inhibits the production and/or the effect of estrogens. The substance can be an anti-estrogen, aromatase inhibitor or both. The method is further drawn to improving the appearance of a body region. The claims of '526 are a specie of the instant claims because the action of applying an anti-estrogen and/or an aromatase inhibitor to skin to treat cellulite inherently practices the steps of the instant claims and results in the instantly claimed result of improving body appearance. The method of '526 falls within the scope of instant claim 27 regarding the stabilization, increase or restoration of collagen because said limitations are inherent properties of anti-estrogens and aromatase inhibitors and their effect will naturally occur when the claimed method of '526 is practiced.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-45 and 47-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 27 is rejected because the phrase "administering an effective amount of a substance" is vague. It is unclear to whom the substance is being administered. It is suggested the phrase be changed to "administering to said mammal an effective amount of a substance."

Claim 33 is rejected because the phrase "The method use according" is confusing. It is suggested that "use" be deleted.

Claim 35 is rejected because the phrase "the substance has both an inhibitory effect on aromatase and on 5-alphja-reductase" is vague and indefinite. It is not clear what the nature of the inhibitory effect is. Does the substance inhibit the enzymatic activity, inhibit a binding interaction or some other effect? Further the wording of

the phrase is confusing. "Both an inhibitory" implies that the substance exhibits some other effect as well. It is suggested that the phrase be changed to "the substance inhibits the catalytic activity of aromatase and 5-alpha-reductase."

Claim 38 is rejected because the phrase "improving appearance of a body region" is vague and indefinite. The nature of the improvement is unclear. Further, does body region mean internally and externally? The metes and bounds of the body region and the improvement in appearance are undefined.

Claim 39 is rejected because the phrase "dentine and the vessel walls of the arteries" is confusing because "dentine" is related to teeth. It is unclear if "dentine" and "vessel walls of arteries" are somehow combined. If not, it is suggested that the phrase be changed to "dentine, vessel walls of arteries."

Claim 47 is rejected because the term "upper" is a relative term and no comparison is made. It is unclear to what part of the body "upper" refers.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 27-40 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Schmidt et al. (US 5,945,109).

Schmidt et al. disclose a method of administering a topical formation of a substance that inhibits the formation and/or action of estrogens for treating disorders of the subcutaneous connective fatty tissue, such as cellulite, to improve the appearance of a body region having cellulite (abstract of referenced patent). This disclosure

meets the limitations of instant claims 27 and 38 because a substance that inhibits the action of estrogen is administered to a mammal for the purpose of treating connective tissue and improving the appearance of improving the appearance of a body region. Schmidt et al. did not teach that the estrogen inhibitor has the claimed effects on collagen which aid in its pharmacological effect for the purpose of improving the appearance of a body region. However, these claimed effects do not make the instant claims patentable over the prior art because the estrogen inhibitor's effects on collagen is an inherent property of the compound.

> MPEP 2112.02: PROCESS CLAIMS — PRIOR ART DEVICE ANTICIPATES A CLAIMED PROCESS IF THE DEVICE CARRIES OUT THE PROCESS DURING
>
> Under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device. When the prior art device is the same as a device described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process. In re King, 801 F.2d 1324, 231USPQ 136 (Fed. Cir. 1986) See also In re Best, 562F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) Ex parte Novitski, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993

Further, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

The substance can comprise an anti-estrogen such as Tamoxifen (col. 4, lines 45-51 of the referenced patent), as required by instant claim 28. Alternatively, the substance can be an aromatase inhibitor such as 4-hydroxyandrostenedione (col. 3, lines 40-50 of the referenced patent), as required by instant claims 28 and 29. The compound 4-hydroxyandrostenedione is also inherently a 5-alpha reductases inhibitor and would therefore inhibit the production of dihydrotestosterone, as required by instant claims 34-36. The aromatase inhibitor can also be obtained from soya glycins. The soya glycins can be oxidized, as required by instant claims 30 and 31 (col. 4, lines 17-45, of the referenced patent). The substance can be administered in the form of a cream wherein the active agent is oxidized soya glycins in an amount of 0.35 g in a cream having a mass of 100.0 g. Thus, the soya glycins would constitute 0.35% of the cream, which falls within the claimed range of 0.1 to 5% of instant claim 32 (col. 6, Ex. 1 of the referenced patent). An anti-estrogen can be added to the cream comprising the oxidized soya glycins and this mixture can be applied to treat connective tissue, which meets the limitation claim 33 for the application of a mixture comprising an anti-estrogen and an aromatase inhibitor (claim 4 of the referenced patent) . As noted in the abstract and in column 7 of the referenced patent, the substance can be applied to a specific body region by topical administration, thus meeting the requirements of claims 37 and 40. The disclosure of Schmidt et al. also meets the

limitation of claim 39 because applying the claimed substance to the skin would inherently impart some of the substance to collagen in the skin. Thus, the estrogen inhibiting effects of the substance would stabilize collagen in the skin while also treating cellulite.

Claims 27, 28 and 45 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Fritz et al. (Endocrine (1998) 139(8): 3399).

Claim 27 is drawn to a method of stabilizing, restoring or increasing collagen in a mammal by administering an effective amount of a substance that inhibits the production and/or the effect of estrogens. This claim is interpreted to mean that any reference that discloses the administration of a substance that has the claimed properties regarding collagen meets the claim because the substance will exert its effect, absent any showing of objective evidence. Any mammal taking in a substance that has an effect on estrogen levels will experience that property because a substance and its properties are not separable.

Fritz et al. disclose that Tamoxifen attenuates the effects of exogenous glucocorticoid on bone formation and growth in piglets. Dexamethasone, a glucocorticoid, was administered to growing piglets and caused said piglets to experience a reduction in bone growth velocity and axial growth. Tamoxifen, an anti-estrogen as required by instant claims 1 and 2, was then co-administered with the dexamethasone and caused a reduction in the negative effects of the glucocorticoid on the piglets. This disclosure meets the limitations of claim 1 because an anti-estrogen was administered to a mammal. Any mammal receiving Tamoxifen inherently practices the claimed method because a compound and its properties are not separable. The mammal will inherently experience a restoration or increase in collagen. Claim 45 is anticipated because Tamoxifen was administered to a mammal to decrease the side effect associated with the therapeutic use of a glucocorticoid.

Claims 27, 28, 39, 41, 43 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Grainger et al. (US 5,770,609).

Grainger et al. disclose a method for treating or preventing atherosclerosis, thrombosis, myocardial infarction and stroke by administering a compound of formula I (col. 2, lines 60-68-col. 2, lines 1-20). A preferred embodiment of the compound of formula I is Tamoxifen, an anti-estrogen agent (col. 7, lines 42-50). This

disclosure meets the limitation of claims 27 and 28 because Tamoxifen is an anti-estrogen that is being administered to a mammal and it affects the vessel walls of arteries, as required by claim 39, for the treatment of the conditions of claims 41, myocardial infarction and brain infarction. According to Webster's Dictionary, an infarction causes tissue necrosis due to insufficient blood supply (p. 626). A stroke meets this definition since the flow of blood to the brain is interrupted by the stroke. The disclosure also meets the limitation of claim 43 for the treatment of arteriosclerosis. According to Webster's Dictionary, atherosclerosis is a form of arteriosclerosis characterized the by the deposit of lipid materials in cell walls (p. 134). Grainger et al. did not teach that Tamoxifen has the claimed effects on collagen which aid in its pharmacological effect for the treatment of brain infarction, myocardial infarction or arteriosclerosis. However, these claimed effects do not make the instant claims patententable over the prior art because Tamoxifen's effect on collagen are inherent to the compound. MPEP 2112.02 *vide supra.* Further, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Claims 27, 28, 39 and 42 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Nikura et al. (US 5,254,594).

Nikura et al. teach that Tamoxifen is a remedy for osteoporosis (col. 2, 1-15 of the referenced patent). This disclosure meets the limitations of instant claims 27 and 28 because Tamoxifen is an anti-estrogen that is administered to a mammal for the purpose of treating osteoporosis, as in instant claim 42. Nikura et al. did not teach that Tamoxifen has the claimed effects on collagen or bone, as in instant claim 39, which aid in its pharmacological effect for osteoporosis therapy. However, these claimed effects do not make the instant claims patententable over the prior art because Tamoxifen inherently exerted its effects on collagen present in the bone because it is a property of the compound. MPEP 2112.02 *vide supra.* Further, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Claims 27, 28, 39 and 42 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Sannti et al. (US 5,972,921).

Sannti et al. teach treating detrusor urethral sphincter dyssynergia in men by administering effective amount of an aromatase inhibitor (abstract of the referenced patent). Formetane® which is a trade name for 4-hydroxyandrostenedione (col. 7, line 33 of the referenced patent), is a preferred aromatase inhibitor. Urinary incontinence is a consequence of a dysfunctional urethral sphincter. Thus, administration of an aromatase inhibitor will inherently treat incontinence. This disclosure meets claims 27 and 29 because Formestane is an aromatase inhibtor which is administered to treat incontinence, as required by instant claim 44. Formetane® is also a 5-alpha reductases inhibitor which decreases the effect of dihydrotestosterone, as required by instant claims 34-36. Sannti et al. did not teach that Formetane® has the claimed effects on collagen present in urinary passage ways, as in instant claim 39, which aid in its pharmacological effect for urinary incontinence therapy. However, these claimed effects do not make the instant claims patententable over the prior art because Formetane® inherently exerted its effects on collagen residing in urinary passage ways because it is a property that was always present in the compound. MPEP 2112.02 *vide supra.* Further, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Claims 27, 28, 37-40, 47 and 48 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Tanabe et al. (US 6,455,517).

Tanabe et al. teach treating estrogen-dependent skin atrophy by topically administering effective amount of an anti-estrogen such as a compound having a 1, 3, 5-estratriene nucleus which is substituted at the C-17 or C-11 position (abstract of the referenced patent), thus meeting the requirements of claims 27, 28, 37, 38 and 40. Symptoms of dermal atrophy include facial wrinkles and are due to such factors as aging and damage from the sun (col. 83, lines 30-68 of the referenced patent), which meets the limitations of claims 47 and 48. Tanabe et al. did not teach that administration of the anti-estrogens stabilizes, restores or increases collagen in the skin, as in instant claim 39. However, these claimed effects do not make the instant claims patentable over the prior art because anti-estrogenic compounds inherently exerted their effects on collagen residing in the skin because those properties are

inherently present in the compound. MPEP 2112.02 *vide supra.* Further, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27, 28, 37-40, 47 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanabe et al. (US 6,455,517).

The disclosure of Tanabe et al. is discussed *supra.* Further, Tanabe et al. identify Tamoxifen as a well known anti-estrogen that has the same effects as the claimed 1, 3, 5-estratriene compounds and use it as a standard to compare anti-estrogenic activity (co. 80-81 of the referenced patent).

Tanabe et al. do not specifically disclose the administration of Tamoxifen for treatment of facial wrinkles or ameliorating the effects of the sun on the skin.

However, it would have been obvious to one of ordinary skill in the at the time the invention was made to use Tamoxifen for this purpose because it is an anti-estrogen and will inherently cause a restoration or increase in collagen in a mammal. Tanabe et al. provide the motivation to choose a compound having a 1, 3, 5-estratriene

nucleus which is substituted at the C-17 or C-11 position to treat facial wrinkles. Tamoxifen is a functional equivalent to the anti-estrogenic compounds having a 1, 3, 5-estratriene nucleus taught. Thus, the ordinary artisan would have had a reasonable expectation that Tamoxifen could be used to treat estrogen-dependent skin atrophy because it has anti-estrogenic activity equivalent to the compounds taught by Tanabe et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
Examiner
1651

JEAN C. WITZ
PRIMARY EXAMINER